Remarks/Arguments:

Claims 1-24 and 26 are pending. Claims 4, 5, 16-24 are withdrawn. Applicants have amended claim 1, as supported throughout the specification, for example, at pg. 25, lines 26 and 27 of the substitute specification. No new matter has been added.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-3 and 6-15 stand rejected as allegedly failing to comply with the written description requirement. The Office Action states "absent a physical separator between indicator zones" is not supported by the specification. Claim 1, however, was previously amended to recite "absent a physical *divider* between indicator zones." Nevertheless, this concept is inherently supported in the specification. There is no *in haec verba* (exact language) requirement, and support may be express, implicit or inherent disclosure. See M.P.E.P. § 2163(I)(B). Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80 (Fed. Cir. 1986). See also M.P.E.P § 2163(II)(A)(2).

The specification generally, and more particularly the drawings, make clear that the claimed devices do not include a physical divider between indicator zones, and that a sample is capable of freely flowing through from the application zone to the absorption region through more than one indicator zone. Applicants refer, for example, to pg. pg. 18, lines 5-19 (paragraph [0051] of the published application) and Figures 3-6 as supporting this feature. Paragraph [0051] describes sealing elements, designated in the figures by the number 4. Paragraph [0051], describes sealing elements as liquid barriers. The Figures show in three dimensions the presence of these liquid barriers downstream of the application zone. And, the Figures clearly show the *absence* of such liquid barriers between indicator zones. Therefore, the specification makes clear that the claimed devices do not include a physical divider between indicator zones. Accordingly, Applicants had possession of the claimed invention at the time of the invention. The rejection, therefore, should be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-3 and 6-15 stand rejected as allegedly indefinite. With respect to claim 1, the Office Action states that "are used" should be removed from claim 1. In the previous

amendment, this language was removed. Accordingly, this rejection is improper and should be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1-3, 6, 7, 9 and 11-15 stand rejected as obvious over U.S. Pat. No. 6,103,536 ("Geisberg") in view of U.S. Patent No. 6,855,561 ("Jerome"). Claims 8 and 9 stand rejected as obvious over Geisberg in view of Jerome and further in view of U.S. Pat. No. 4,943,522 ("Eisinger"). Claims 1-3, 6-11 and 13-15 stand rejected as obvious over U.S. Patent No. 5,559,041 ("Kang") in view of Jerome and Eisinger. These rejections do not establish *prima facie* obviousness because the proposed combination of references do not provide all of the features of the claimed invention.

Claims 1-3, 6, 7, 9 and 11-15 - Geisberg in view of Jerome

First, Geisberg and Jerome, alone or in any reasonable combination, fail to disclose or suggest that the erythrocyte can serve as both the indicator particle and the analyte. Claim 1, as currently amended, recites "the erythrocyte serves as both the indicator particle and the analyte."

Geisberg relates to a device for the detection of at least one analyte in a sample solution, comprising a solid support containing a sample application zone, a particle zone, and at least one signal ratio area comprising a first and a second signal zone. The particles in the particle zone are described as a wide range of materials known in the art and mention erythrocyte ghosts. Col. 5, lines 17-29 of Geisberg. Geisberg further describes the types of analytes that may be detected such as antigens and antibodies. See col. 11, line 63 to col. 12, line 55 of Geisberg. Geisberg, however, does not disclose or suggest that the erythrocyte is the analyte as well as the indicator particle. Thus, prior to claimed invention, it was generally understood that erythrocytes represented either analytes or were used separately as indicator particle to detect other analytes. The claimed invention, however, recites that erythrocytes contained in the sample which carry the analytes at the same time serve as indicator particles. See pg. 25, lines 23-30 of the substitute specification.

Jerome does not remedy the deficiencies of Geisberg. Jerome discloses a test device for determining the presence or absence of an analyte in a fluid sample comprising a matrix comprising a sample receiving zone, a label zone, and an observation area. Jerome describes a "label" which is capable of producing a signal that is detectable by visual or instrumental means, such as erythrocytes or erythrocytes ghosts. Col. 7, line 58 to col. 8, line 3 of Jerome.

Jerome also describes an "analyte" as the compound or composition to be detected, such as toxins or proteins. Col. 7, lines 14-40 of Jerome. Jerome, however, does not disclose or suggest that the erythrocyte is the analyte as well as the indicator particle.

Thus, a skilled person upon reading Geisberg and Jerome and even combining the teachings thereof would not arrive at the device as claimed. Accordingly, *prima facie* obviousness has not been established, and withdrawal of the rejections is warranted.

Second, Geisberg fails to disclose or suggest that the two indicator zones are positioned on the membrane substantially parallel and the indicator zones bind the cellularly bound analyte and an analyte comprising an erythrocyte in the liquid sample. Claim 1 recites, in part, "the at least two indicator zones are positioned on the membrane substantially parallel . . . the at least two indicator zones comprise a first indicator zone containing a bonding element for binding the cellularly bound analyte and the at least two indicator zones comprise a second indicator zone containing a binding element for binding an analyte comprising an erythrocyte in the liquid sample."

Geisberg requires that the device has two signal zones in series, and sets forth as *imperative* that the sample passes sequentially through each signal zone. Geisberg discloses that each signal ratio is comprised of a first and second signal zone. See col. 3, lines 45 and 46 of Geisberg. Geisberg explains:

> It should be noted that in the present device, the sample application zone, the particle zone, and the one or more signal ratio areas are arranged in fluid communication such that a sample solution flows **sequentially** through the sample application zone, the particle zone, and then through the first and **subsequently** the second signal zone of each signal ratio area. Col. 3, lines 54-60 of Geisberg (emphasis added).
>
> Thus, for the detection of more than one analyte, a strip with a sample application zone, a particulate zone, and more than one signal ratio areas are arranged **sequentially along the length of the strip**. Alternatively, for each analyte, a **separate series** of particulate zones and signal ratio areas can be placed in parallel on one comparatively wide strip. Col. 8, lines 20-26 of Geisberg (emphasis added).

Additionally, Figures 2-5 of Geisberg show the sequential arrangement of the inverse signal zone (13) and the direct signal zone (15) of the signal ratio area. Thus, Geisberg discloses the determination of a single analyte, in which one signal ratio area is needed comprising a first and second signal zone and the signal zones are arranged sequentially along the length of the strip. Accordingly, Geisberg fails to disclose or suggest that the two indicator zones are

positioned on the membrane substantially parallel and the indicator zones bind the cellularly bound analyte and an analyte comprising an erythrocyte in the liquid sample.

Third, Applicants submit that those of skill in the art would not have combined the teachings of Jerome with Geisberg because such a combination would render Geisberg unsatisfactory for its intended purpose. Geisberg requires that samples pass sequentially through indicator zones. Even though a separate series of particular zones and signal ratio areas can be placed in parallel, for each analyte, the two signal zones have to be arranged sequentially. As emphasized in Geisberg:

> It is **imperative** that the particles and the sample solution suspected of containing the analyte first go through the first signal zone before entering the second signal zone. Col. 12, lines 63-66 of Geisberg (emphasis added).

The labels disclosed in Jerome, therefore, are not suitable for the device disclosed in Geisberg requiring passing samples sequentially through indicator zones. For these reasons, the skilled artisan would not combine these references as proposed in the Office Action. The Office Action has thus not provided a proper reason to combine the references, and therefore has not established *prima facie* obviousness.

Fourth, Geisberg teaches away from the claimed invention because Geisberg relates to detection of soluble molecules, which is not suitable for detection of a cellular analyte. Claim 1 recites, in part, "at least one of the plurality of analytes is a *cellularly bonded analyte*, in a liquid sample." The analyte to be determined by Geisberg are *soluble* molecules with a molecular weight range between 100 and about 100,000 (or higher molecular weight). See col. 11, line 63 to col. 12, line 55 of Geisberg. Geisberg recites a "sample solution" in claim 1. A person skilled in the art would understand that a cellularly bonded analyte is a cell-containing liquid, which is not a *solution*, but rather a *suspension*. Thus, one skilled in the art would know that a device used for detection of soluble molecules would not be suitable for detection of a cellular analyte. Accordingly, one skilled in the art would not consider the teachings of Geisberg for determination of a cellular analyte.

Additionally, Applicants note that Jerome is directed to detection of the presence or absence of a single analyte. However, a device for determining the presence or absence of a single analyte would not automatically be suitable for determining a plurality of analytes.

For all the foregoing reasons, Applicants respectfully submit a *prima facie* case of obviousness has not been established, and claim 1 should be in condition for allowance. Claims

2, 3, 6-15, and 26 depend, directly or indirectly, from claim 1, and therefore should each be allowed for at least the reasons set forth above.

Claims 8 and 9 - Geisberg in view of Jerome and Eisinger

For the reasons presented above, Geisberg and Jerome, even as combined, would not arrive at the device as claimed. Eisinger does not remedy the deficiencies of Jerome or Geisberg. Eisinger discloses a device and method for detecting blood group antigens. Eisinger does not disclose or suggest that the erythrocyte is the analyte as well as the indicator particle. Additionally, Eisinger does not disclose use of at least *two* types of indicator particles of which at least one type being erythrocytes, nor does Eisinger disclose a single membrane comprising a first indicator zone contains a bonding element for binding a cellularly bound analyte and a second indicator zone containing a bonding element for binding an analyte contained in plasma on the same membrane.

Additionally, while Eisinger relates to the determination of cellularly bonded analytes, it teaches away from the claimed invention. Eisinger mentions that for the determination of cellular and plasmatic parameters, the cells have to be removed before determining the plasmatic parameters (see Example 3, column 22, lines 60 to 68). In addition, Eisinger applies the plasma separated from the cells for the typing of the antibodies using known donor erythrocytes, which again teaches away from the claimed invention. Eisinger requires a separation step of plasma from cells, which is not required by the claimed invention.

Thus, a skilled person upon reading Geisberg, Jerome, and Eisinger and even combining the teachings thereof would not arrive at the device as claimed. Accordingly, *prima facie* obviousness has not been established, and withdrawal of the rejection is warranted.

Claims 1-3, 6-11 and 13-15 - Kang in view of Jerome and Eisinger

Claims 1-3, 6-11, and 13-15 stand rejected over Kang in view of Jerome and Eisinger. For the reasons presented above, Jerome and Eisinger would not arrive at the device as claimed. Kang does not remedy the deficiencies of Jerome or Eisinger. Kang discloses an immunochemical assay device comprising a base membrane with (i) a reservoir pad; (ii) a wicking membrane with two indicator zones; and (iii) *at least one filter zone.* The filter element disclosed in Kang is used to trap unwanted components in the fluid sample, especially as a controlled cell lysing system. Kang explains:

> For example in an immunstatus assay performed on a sample of whole blood it is advantageous to select as the second filter element a

> membrane which would maintain the integrity of whole blood cells while serum migrates through. This prevents the discoloration associated with blood cell lysis from spreading into the assay indicia zone. Col. 5, line 54 to col. 6, line 4 of Kang.

Thus, the device of Kang is not suitable for determination of a plurality of analytes, wherein at least one analyte is a cellularly bonded analyte. A person skilled in the art would not consider using the device of Kang in the claimed invention for simultaneous and qualitative or quantitative determination of a plurality of analytes, wherein at least one analyte is a cellularly bonded analyte. Therefore, a skilled person at the time of the invention, even combining the teachings of Kang, Jerome, and Eisinger, would not reach the device as claimed. Accordingly, *prima facie* obviousness has not been established, and withdrawal of the rejections is warranted.

Double Patenting

Claims 1-5 and 7-15 stand provisionally rejected on the grounds of nonstatutory obviousness-type double patenting over claims 1-9 of co-pending U.S. Application No. 10/563,659 in view of Jerome. Applicants request that the rejection be held in abeyance pending an indication of allowable subject matter.

Conclusion

Applicants respectfully request reconsideration and withdrawal of the various rejections in light of the amendments and remarks made herein. A notice of allowance is requested.

Respectfully submitted,

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